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10/669,861

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Dong-Ki Lee

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FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER

DUNSTON, JENNIFER ANN

ART UNIT

PAPER NUMBER

1636

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|-----------------------------------|--|
| Office Action Summary | Application No. 10/669,861 | Applicant(s) LEE ET AL. | |
| | Examiner Jennifer Dunston | Art Unit 1636 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,3,5,6,14,22-27,30,31 and 36-41 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6 and 14 is/are allowed.
- 6) ☒ Claim(s) 2,3,5,22-24,30,31 and 36-41 is/are rejected.
- 7) ☒ Claim(s) 25-27 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 June 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The finality of the last Office action is withdrawn. New grounds of rejection are presented herein. This action is in response to the reply filed 5/19/2008.

Currently, claims 2-3, 5-6, 14, 22-27, 30, 31 and 36-41 are pending.

Election/Restrictions

Applicant elected Group I without traverse in the reply filed on 12/22/2005. Currently, claims 2-3, 5-6, 14, 22-27, 30-31 and 36-41 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-3, 5, 22-24, 30-31 and 36-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated transcription factor that comprises a first, second and third zinc finger domain in this order, and an activation domain, wherein presence of the transcription factor in a vertebrate cell can alter the differentiation state of the cell and the DNA contacting residues of the first, second and third domains are as recited in claim 5, does not reasonably provide enablement for transcription factors that do not contain a transcriptional activation domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

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Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The claims are drawn to a transcription factor containing the following zinc finger domains in the recited order: glutamine at position -1 of the first zinc finger domain; serine at position 2 of the first zinc finger domain; asparagine at position 3 of the first zinc finger domain; and arginine at position 6 of the first zinc finger domain (abbreviated herein as QSNR); (ii) glutamine at position -1 of the second zinc finger domain; serine at position 2 of the second zinc finger domain; asparagine at position 3 of the second zinc finger domain; and lysine at position 6 of the second zinc finger domain (abbreviated herein as QSNK); and cysteine at position -1 of the third zinc finger domain; serine at position 2 of the third zinc finger domain; asparagine at position 3 of the third zinc finger domain; and arginine at position 6 of the third zinc finger domain (abbreviated herein as QSNR). The transcription factor must be capable of altering the differentiation state of the cell. Claim 2 requires the transcription factor to induce a neuronal phenotype. Claim 3 requires the transcription factor to induce neurite extension, and claim 3 requires the transcription factor to induce neurite extension in a mouse neuroblastoma cell.

Breadth of the claims: The claims are broad in that they do not specifically require the presence of an activation domain.

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Guidance of the specification and existence of working examples: The specification teaches the amino acid sequence of Neuro1-p65 chimeric zinc finger protein (SEQ ID NO: 2). The specification teaches that the polypeptide of SEQ ID NO: 2 is capable of inducing neurite formation in Neuro2a cells (e.g. Figure 8). The Neuro1-p65 protein of SEQ ID NO: 2 is composed of the zinc finger domains QSNR-QSNK-CSNR and the p65 activation domain (e.g. paragraph bridging pages 48-49). The QSNR-QSNK-CSNR preferably binds to a sequence of GAA-GAA-GAA (e.g., Table 2). No evidence is provided in the present specification that a transcription factor comprising the QSNR-QSNK-CSNR motif without an activation domain is capable of altering the differentiation state of any vertebrate cell, inducing a neuronal phenotype in a vertebrate cell, or inducing neurite extension in a vertebrate cell or, more specifically, a mouse neuroblastoma cell.

To identify the polypeptide of SEQ ID NO: 2, Applicant screened three-finger and four-finger zinc finger protein transcription factor (ZFP-TF) libraries, constructed using 40 and 25 zinc finger domains respectively (e.g. Example 1; page 108, last paragraph). The zinc finger proteins were expressed as fusions with a p65 transcriptional activation domain and to the KRAB repression domain (e.g. page 108, last paragraph). To screen for ZPF-TF capable of inducing neuronal differentiation, Neuro2A cells were transiently transfected with library plasmids and assayed for neuritogenesis (e.g. page 109). The specification asserts that several ZFP-TFs were identified, with Neuro1-p65 having the most prominent effect on differentiation (e.g. page 109). Further, the specification teaches that mutations that disable the binding activity of the zinc finger domains of Neuro1-p65 abolish its ability to support neurogenesis (e.g. page 110). The specification does not describe the sequence of the ZFP-TFs capable of inducing neural

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differentiation, except for Neuro1-p65 (SEQ ID NO: 2). Thus, the working example does not provide evidence that the claimed zinc finger domains will have the same function when operably linked to a repression domain or when a regulatory domain is absent.

Predictability and state of the art: The prior art teaches that zinc finger transcription factors can be used to activate or repress transcription (Barbas, III et al, US Patent No. 6,242,568 B1, cited on the IDS filed 11/26/2004). Transcription factors that do not contain a regulatory domain may be used to compete with a native zinc finger binding protein at a promoter, for example (Barbas, III et al, paragraph bridging columns 7-8). Given that the specification teaches that the protein of SEQ ID NO: 2 activates transcription of a gene to induce neurite formation in Neuro2a cells, it would be unpredictable to use the zinc finger domains operably linked to a repression domain to induce neurite formation or in a repressive manner.

Amount of experimentation necessary: The quantity of experimentation necessary to use the claimed zinc finger protein without an additional activation domain is large. The specification does not teach the genes activated by the transcription factor of SEQ ID NO: 2. The specification does not teach genes whose expression normally induces differentiation or neurite formation but are repressed by a transcriptional repressor that could be competed away with the claimed zinc finger domains. Thus, a large amount of experimentation would be required to identify conditions under which the zinc finger domains would be capable of altering the differentiation state of a cell without an activation domain.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an

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undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 2-3, 5, 22-24, 30-31 and 36-41 are not considered to be fully enabled by the instant specification.

Response to Arguments - 35 USC § 103

Applicant's arguments, filed 5/19/2008, with respect to the rejection of claims 2-3, 5, 6, 14, 22-27, 30-31 and 36-41 under 35 U.S.C. 103(a) as being obvious over Kim et al in view of Liu et al have been fully considered and are persuasive. The previous rejection of claims 2-3, 5, 6, 14, 22-27, 30-31 and 36-41 has been withdrawn.

Conclusion

Claims 6 and 14 are allowed.

Claims 25-27 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached at 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

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may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

/JD/

/Celine X Qian Ph.D./
Primary Examiner, Art Unit 1636